people or attempting to redefine them as social problems, and therefore outside the remit of medicine.

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Genetics and medicalisation

Genetics could drive a new wave of medicalisation if genetic tests are accepted without appropriate clinical evaluation

In the public imagination genetic science has already brought us close to a world in which tests and cures are available for most diseases. The immediate prospects are, however, decidedly more prosaic. With the exception of the relatively rare high penetrance, single gene disorders, genetic tests differ little from most other medical tests, providing evidence of statistical risk only. Inflated perceptions of the value of specific genetic tests could drive a wave of inappropriate medicalisation. Genetic claims, tests, and treatments, like others, should be subjected to evaluation to establish their clinical usefulness, so that doctors and patients can act on sound evidence.

The term "genetics" conveys two different concepts: genetics as the study of inherited characteristics, and genetics as the study of cellular processes controlled by DNA. DNA codes lie at the centre of the biological processes in all living cells and generate the protein building blocks for cellular activity. Variations in coding abound between people. The differences occasionally derive from variations in a single gene, but much more typically they derive from the interacting effects of many genes. DNA is no blind cipher, but part of a modulating system interacting with cellular mechanisms and environmental factors, that together time and modify the expression of proteins within the cells that make up the human organism.[1]

In the public mind, high penetrance, single gene disorders, such as Huntington's disease, dominate the image of genetics and genetic testing and are a stereotype of inevitable future disaster.[2] Fortunately this stereotype is misleading when applied to the more common multifactorial conditions and even to many single gene disorders that often show considerable variation in clinical manifestations. The thalassaemias, for example, show great phenotypic variation, with a variety of factors—environmental and genetic—influencing eventual outcome.[3]

The genes that play a part in the pathogenesis of most common disorders are for the most part as yet unidentified and their role ill understood. Individually their predictive value is low, and at present there is little to suggest that they will have any greater clinical value than more conventional physiological risk markers, such as blood pressure or cholesterol concentrations. We believe, as do others, that the arguments for "genetic exceptionalism"—for treating genetic information and tests as somehow special—are not compelling.[4 5] Outside the high penetrance, single gene disorders, genetic tests, like most other medical tests, provide evidence only of statistical risks.

Most physiological deviations are continuously distributed in the population, and most pathological processes give rise to a range of severity in clinical signs and symptoms.[6] Clinical practice requires the establishment of agreed cut off points to identify disease and to separate people for whom treatment should be beneficial from other patients for whom the risks of diagnosis or treatment might outweigh the benefits.

Over time, the tendency has been to expand diagnostic and treatment boundaries, and to include in the "disease" category people with milder manifestations of pathology and lower levels of risk. Genetic tests for markers that may not result in symptoms for half a century or more could be new examples of a process of premature medicalisation—of attaching the "disease" label before it has been established that prevention or treatment is clearly beneficial. Treating the presence of a genetic marker as though it were the clinical disease can be very unhelpful. In haemochromatosis, less than 1% of homozygotes for the responsible genetic variant develop frank clinical manifestations.[7]

New testing technology is creating inexpensive ways of identifying differences in many genetic sequences all at once, but as yet there is little clinical value in knowing about such polymorphisms. Epidemiology and clinical trials will be needed to test claims linking genetic variants to disease. Unless it is established that a genetic variant is a pointer to beneficial action, there is a potential for inappropriate medicalisation through the spread of poorly understood tests. The perceptions of risk resulting from such tests may bear little relation to the scientific facts and uncertainties. Inflated ideas about risks could result in people carrying such polymorphisms being treated unfairly in many areas, including employment or insurance.[8]

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On a fundamental level, genetic science is forcing a re-examination of the concept of normality itself, by showing that everyone's genome is different and that we are all in some sense "abnormal." We each carry genetic variants, many of which will have no detectable impact in normal circumstances, but some undoubtedly will alter our risk of disease or may, with a partner carrying similar variations in their genomes, result in the birth of a child with a recessive genetic disorder.

Genetics also raises interesting questions about causation and about responsibility for adverse health events. For example, do people with a genetic predisposition such as factor V Leiden who develop venous thrombosis on long haul flights do so because of genetic susceptibility or because of the flight itself?[9] Is the airline or the person at fault? To what extent should society regulate to ensure a safe environment only for the majority? Or should the standards be set so that all people with susceptibilities are protected?

Seeking commercial rewards from new medical tests or treatments is not new; it is often productive, provided the tests and interventions are effective and the profits are reasonable. But quite often these standards are not met. The enormous investments needed to exploit genetics may have driven a more exuberant set of claims than usual, designed to appeal not only to the public but also to investors. Each new technology brings a crop of exaggerated claims. Even the discovery of radioactivity led to a new batch of "cure all" patented medicines, which enjoyed considerable popularity until the death of the American tycoon E M Byers of radium poisoning in 1932.[10] The appeal of medical "snake oils" is an enduring attribute of human gullibility, not of genetic science.

The antidote to genetics as a driver of medicalisation lies in remaining sceptical and level headed. Genetic claims, tests, and products should be treated in the same way that other medical markers and interventions are increasingly treated: with rigorous evaluation. The successful management of genetic medicalisation will depend on clinical evaluation, integrity, and transparency and on providing accurate information to consumers and patients. Public education about interventions based on genetic science will also be needed to prevent inappropriate social responses that may either lead to discrimination or, conversely, prohibit the adoption of tests and treatments that can reduce or prevent disability. Genetic technologies have the potential to be of major benefit to society, but their introduction must be measured, attentive to the social and ethical considerations of the day, and, most importantly, based on best evidence.

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Medicalisation, limits to medicine, or never enough money to go around?

Spending on preventive treatments that help a few is unaffordable

Ivan Illich, in *Limits to Medicine*, commented: "The more time, toil and sacrifice spent by a population in producing medicine as a commodity, the larger will be the by product, namely the fallacy that society has a supply of health locked away which can be mined and marketed."[1] Rich Western societies are investing in preventive treatments that will benefit only a minority of those who take them for a long time, a situation well illustrated by the statins. Widespread use of statins is scarcely affordable in the developed world and unachievable in developing countries, although the drugs are still marketed heavily there. Using resources to purchase statins means other effective treatments may not be available.

From the perspective of the pharmaceutical industry, statins are an ideal group of drugs. They are, with one exception, safe and free from common side effects. They achieve a premium price and potentially have an increasingly wide market in the primary and secondary prevention of cardiovascular disease. About 11.5 million adults (5.4% of the adult population) in the United States are currently taking either atorvastatin, simvastatin, or pravastatin, all of which are in the top 40 most commonly prescribed pharmaceuticals in the United States.[2] Indeed, atorvastatin (Lipitor) is now the biggest prescription-only drug in the world.

It is paradoxical that while achieving benefits in reducing mortality and major morbidity, the statins are the latest drugs to present a major challenge for health policy.[3] Medical research in the late 20th century has helped define the effectiveness of many medicines, particularly in areas of chronic disease such as cardiovascular medicine and oncology. In developed countries, it is in the prevention of disease that most research now takes place. Treatment for acute health problems, particularly those found predominantly in

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